CLAIMS

1. A method for detecting the presence of wild-type p53 protein in a cell, comprising the steps of:

contacting a p53-specific binding DNA fragment with a cell lysate from a tissue of a human, to bind the DNA fragment to wild-type p53 present in the cell lysate;

detecting the presence of wild-type p53 protein in the cell by detecting binding of the DNA fragment to wild-type p53.

2. The method of claim 1 wherein the p53-specific binding DNA segment comprises nucleotides 103 to 134 as shown in SEQ ID No:1.

3. The method of claim 1 wherein the p53-specific binding DNA segment comprises nucleotides 104 to 123 as shown in SEQ ID No:1.

4. The method of claim 1 wherein the p53-specific binding DNA fragment comprises more than one monomer of the sequence 5'-RRRCWWGYYY-3'.

5. The method of claim 1 wherein there are from 0 to 40 nucleotides between said monomers.

6. The method of claim 1 wherein the DNA fragment is labelled with a detectable moiety selected from the group consisting of: a radioactive moiety, a colorimetric moiety, or a fluorescent moiety.

7. The method of claim 1 wherein the step of determining the amount of p53-specific binding DNA comprises:

immunoprecipitating p53 protein with anti-p53 monoclonal antibodies.

8. A method of detecting the presence of a wild-type p53 protein in a cell, comprising the steps of:

providing a histological section from a human;

incubating the section with a detectably-labeled p53-specific binding DNA fragment to bind said DNA fragment to wild-type p53 present in the histological sample;

removing unbound DNA fragment from the histological section; and

determining the amount of DNA fragment which is bound to the histological sample.

9. The method of claim 8 wherein the p53-specific binding DNA segment comprises nucleotides 103 to 134 as shown in SEQ ID NO:1.

10. The method of claim 8 wherein the p53-specific binding DNA segment comprises nucleotides 104 to 123 as shown in SEQ ID NO:1.

11. The method of claim 8 wherein the p53-specific binding DNA fragment comprises more than one monomer of the sequence 5'-RRRCWWGYYY-3'.

12. The method of claim 11 wherein there are between 0 and 40 nucleotides between said monomers.

13. The method of claim 8 wherein the DNA fragment is labelled with a detectable moiety selected from the group consisting of: a radioactive moiety, a colorimetric moiety, or a fluorescent moiety.

14. A method of providing the physiological effect of wild-type p53 protein to a cell, comprising the steps of:

providing to a cell a compound which is is able to complex specifically with a p53-specific binding site.

15. The method of claim 14 wherein the compound comprises a single-stranded , linear or circular, oligonucleotide or oligonucleotide containing nucleotide analogs which can form a complex with a p53 specific DNA binding site.

16. The method of claim 14 wherein the compound comprises a polypeptide.

17. The method of claim 16 wherein the polypeptide comprises all or a part of human wild-type p53 protein.

18. The method of claim 15 wherein the oligonucleotide or oligonucleotide containing nucleotide analogs comprises the monomer sequence RRRCWWGYY or the complement thereof.

19. The method of claim 14 wherein the compound comprises at least a portion of the monomer sequence RRRCWWGYY as well as sequences adjacent to said monomer sequence in the human genome.

20. The method of claim 18 wherein the oligonucleotide or oligonucleotide containing nucleotide analogs comprises more than one monomer of said sequence.

21. The method of claim 18 wherein the oligonucleotide or oligonucleotide containing nucleotide analogs comprises between 0 and 40 nucleotides between said monomers.

22. A double-stranded DNA fragment which comprises a p53-specific DNA binding site, wherein the fragment comprises more than one monomer of the sequence RRRCWWGYYY and wherein the fragment is covalently attached to an insoluble polymeric support.

23. A linear or circular single-stranded oligonucleotide or oligonucleotide containing nucleotide analogs which is able to complex specifically with a p53-specific binding site, said binding site comprising more than one monomer of the sequence RRRCWWGYYY.

24. The oligonucleotide or oligonucleotide containing nucleotide analogs of claim 23 which contains one or more switchback linkers which allow the oligonucleotide to complex with both strands of the p53-specific binding site.

25. The oligonucleotide or oligonucleotide containing nucleotide analogs of claim 23 which is selected from the group consisting of a methylphosphonate, an aminomethylphosphonate, an aminomethylphosphonate, a phosphorothioate, a phosphorodithioate, a substituted or unsubstituted phosphoramidate, an oligoribonucleotide, an oligodeoxyribonucleotide, an alpha-oligonucleotide and mixtures thereof.

26. The oligonucleotide or oligonucleotide containing nucleotide analogs of claim 23 which is terminated at the 3' or 5' end with a moiety which reduces susceptibility to oligonucleotide degradation or facilitates uptake by the cells.

27. The oligonucleotide or oligonucleotide containing nucleotide analogs of claim 26 wherein the moiety is selected from the group consisting of: a substituted or unsubstituted amino moiety, polyethylene glycol, polylysine, acridine, dodecanol, and cholesterol.

28. A method of identifying compounds which specifically bind to p53-specific DNA binding sequences, comprising the steps of:

contacting a p53-specific-binding DNA fragment with a test compound to bind the test compound to the DNA fragment;

determining the amount of test compound which is bound to the DNA fragment.

29. The method of claim 28 wherein soluble DNA fragments are incubated with the test compound and the p53-specific-binding DNA fragment immobilized on a solid support, said soluble DNA fragments not having the ability to specifically bind wild-type p53 protein.

30. A method of identifying compounds which specifically bind to p53-specific DNA binding sequences, comprising the steps of:

contacting a p53-specific-binding DNA fragment immobilized on a solid support with both a test compound and wild-type p53 protein to bind the wild-type p53 protein to the DNA fragment;

determining the amount of wild-type p53 protein which is bound to the DNA fragment, inhibition of binding of wild-type p53 protein by the test compound indicating binding of the test compound to the p53-specific DNA binding sequences.

31. A method of supplying wild-type p53 gene function to a cell which has lost said gene function by virtue of mutation in a p53 gene, comprising:

introducing a wild-type p53 gene into a cell which has lost said gene function such that said gene is expressed in the cell.

32. The method of claim 31 wherein said wild-type p53 gene is expressed to a level higher than any mutant p53 gene present in the cell.

33. The method of claim 31 wherein the introduced wild-type p53 gene recombines with the endogenous mutant p53 gene present in the cell by a double recombination event to correct the p53 gene mutation.

34. A method of supplying a wild-type p53 gene function to a cell which has lost said gene function by virtue of a mutation in a p53 gene, comprising:

introducing a portion of a wild-type p53 gene into a cell which has lost said gene function such that said portion is expressed in

the cell, said portion encoding a part of the p53 protein which is required for non-neoplastic growth of said cell.

35. A method of pre-screening agents for use in cancer therapy, comprising:

measuring the amount of binding of a p53 protein encoded by a mutant gene found in cancer cells of a patient to a DNA molecule which conforms to the consensus binding site having more than one monomer of RRRCWWGYYY;

measuring the amount of binding of said p53 protein to said DNA molecule in the presence of a test substance; and

comparing the amount of binding of the p53 protein in the presence of said test substance to the amount of binding of the p53 protein in the absence of said test substance, a test substance which increases the amount of binding being a candidate for use in cancer therapy.

36. A method of pre-screening agents for use in cancer therapy, comprising:

contacting a transfected cell with a test substance, said transfected cell containing a p53 protein which is encoded by a mutant gene found in cancer cells of a patient and a reporter gene construct comprising a reporter gene which encodes an assayable product and a sequence which conforms to the p53 consensus binding site having more than one monomer of RRRCWWGYYY, wherein said sequence is upstream from and adjacent to said reporter gene; and

determining whether the amount of expression of said reporter gene is altered by the test substance, a test substance which alters the amount of expression of said reporter gene being a candidate for use in cancer therapy.

37. A method of pre-screening agents for use in cancer therapy, comprising:

adding RNA polymerase and ribonucleotides to a transcription construct, said transcription construct comprising a reporter gene which encodes an assayable product and a sequence which conforms to the p53 consensus binding site having at least two monomers of RRRCWWGYYY, said sequence being upstream from and

adjacent to said reporter gene, said step of adding being effected in the presence and absence of a test substance; and

determining whether the amount of transcription of said reporter gene is altered by the presence of said test substance, a test substance which alters the amount of transcription of said reporter gene being a candidate for use in cancer therapy.

38. A DNA construct for use in screening potential chemotherapeutic agents, comprising:

a reporter gene which encodes an assayable product;

a sequence which conforms to the p53 consensus binding site having more than one monomer of RRRCWWGYYY upstream from and adjacent to said reporter gene, wherein said DNA construct is selected from the group consisting of a recombinant plasmid, a viral vector and an isolated molecule of DNA.

39. A method of diagnosing tumor-inducing or hyperplastic-inducing strains of human papilloma virus (HPV) comprising:

contacting cells or cell extracts of patients suspected of being infected by HPV with a p53-specific binding DNA fragment;

detecting the amount of wild-type p53 in said cells or cell extract which binds to said DNA fragment, absence of bound p53 indicating infection by strains of HPV which sequester p53.

40. A method of pre-screening agents for use in cancer therapy, comprising:

contacting a transfected cell with a test substance, said transfected cell containing a wild-type p53 protein and a reporter gene construct comprising a reporter gene which encodes an assayable product and a sequence which conforms to the p53 consensus binding site having more than one monomer of RRRCWWGYYY, wherein said sequence is upstream from and adjacent to said reporter gene; and

determining whether the amount of expression of said reporter gene is altered by the test substance, a test substance which alters the amount of expression of said reporter gene being a candidate for use in cancer therapy.

41. A method of pre-screening oligonucleotides for use in cancer therapy, comprising:

adding a p53 protein which is encoded by a mutant gene found in a cancer patient and a preparation of random oligonucleotides to a p53-specific-binding DNA fragment immobilized on a solid support;

recovering the oligonucleotides which bound to the solid support.